Heart Surgery Forum 2023; 26(6): E817–E825
doi: 10.59958/hsf.6839
https://journal.hsforum.com/

Article

Clinical Efficacy of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Coronary Heart Disease Patients with SYNTAX Score ≥33 and Euro Score ≥6: A Single-Center Retrospective Analysis

Zhiyong Wu[1,*], Xuanlan Chen[1], Yizhong Zhou[1], Nanping Gong[1], Zhitang Chang[1]

[1]Department of Cardiology, Jiangxi Provincial People's Hospital, The First Affiliated Hospital of Nanchang Medical College, 330000 Nanchang, Jiangxi, China
*Correspondence: wuzhiyong76@163.com (Zhiyong Wu)

Submitted: 15 September 2023 Revised: 6 November 2023 Accepted: 7 November 2023 Published: 27 December 2023

Abstract

Objective: To observe clinical efficacy of fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) in coronary heart disease patients with SYNTAX scores (SS) ≥33 and Euro Scores (ES) ≥6 who are unsuitable for or have declined coronary artery bypass graft (CABG). **Methods**: A total of 117 patients with SS ≥33 and Euro Score (ES) ≥6 who were unsuitable for and/or who had declined CABG between Jan 2021 and June 2022 were enrolled in this retrospective analysis. All patients accepted optimal medical therapy and some accepted an FFR-guided PCI procedure. Patients who only underwent optimal medical therapy were divided into the optimal medical therapy group (OMT group) and patients who simultaneously underwent FFR-guided PCI procedure were divided into the PCI group in this retrospective analysis. All patients accepted follow-up for at least 12 months after discharge. **Results**: SS and ES in the two groups were not statistically different ($p > 0.05$). Patients with chronic total occlusion accounted for a greater proportion in the PCI subgroup (31.3%, 5/16) than in other subgroups. Eighteen (18.6%, 18/97) cases in the PCI group developed major adverse cardiac and cerebrovascular events (MACCEs). There were 12 (60%, 12/20) cases of MACCEs in the OMT group, which was statistically different from the PCI group ($p < 0.05$). **Conclusions**: Based on optimal medical therapy, FFR-guided PCI can still have clinical benefit to coronary artery disease patients with SS ≥33 who were not suitable for CABG.

Keywords

fractional flow reserve; percutaneous coronary intervention; SYNTAX score; Euro Score; coronary artery bypass graft

Introduction

The SYNTAX score (SS) can provide guidance for revascularization in coronary heart disease (CHD) patients with left main coronary artery disease, multiple-vessel disease, or both [1,2]. Patients with high-SS ≥33 exhibit significantly greater major adverse cardiac and cerebrovascular events (MACCEs) after percutaneous coronary intervention (PCI) than with coronary artery bypass graft (CABG) surgery.

With the progress of interventional techniques now widely used in coronary interventions, these techniques have been able to further optimize PCI treatment [3–5]. However, there is still a dearth of evidence-based medical recommendations about how to select strategies for the treatment of CHD patients with SS ≥33 and Euro Score (ES) ≥6 who are unsuitable for or decline CABG surgery. Therefore, we retrospectively evaluated the clinical efficacy of fractional flow reserve (FFR)-guided PCI for these patients.

Methods

Study Population

A total of 117 CHD patients with SS ≥33 and ES ≥6 who were unsuitable for or declined CABG in Jiangxi Provincial People's Hospital between January 2021 and June 2022 were studied. Inclusion criteria were as follows: (1) SS ≥33 and ES ≥6. (2) CABG was an unsuitable strategy or patients refused CABG because of higher surgical risk. (3) No contraindications for antiplatelet drugs and PCI. (4) Patients can accept double antiplatelet therapy for at least 12 months. Exclusion criteria were as follows: (1) ST-segment Elevation Myocardial Infarction or non-ST-segment Elevation Myocardial Infarction that needs primary PCI. (2) Severe liver and kidney function (≥3 times the normal upper limit of serum alanine transaminase (ALT), aspartate aminotransferase (AST) and/or serum

creatinine level ≥265 μmol/L). (3) Severe hematological diseases, neurological diseases and malignant tumors. (4) Severe hemodynamic instability such as cardiogenic shock or severe heart failure that would render patients unable to tolerate the procedure. (5) Participation in any other study at the same time. All patients were discussed with the heart team. The heart team was composed of cardiologists, cardiothoracic surgeons, anesthesiologists, intensive care physicians, cardiac catheter interventional doctors and radiologists.

Study Protocols

Baseline evaluations including physical examination, blood biochemical assessment, electrocardiographic (ECG) examination and echocardiographic measurements performed at the time of admission. All patients accepted optimal medical treatment according to the recommendations and requirements named in the guidelines. However, patients that only accepted optimal medical therapy were categorized into the optimal medical therapy group (OMT group), while patients that simultaneously accepted FFR-guided PCI procedure on the basis of optimal medical therapy were categorized into the PCI group. The patients in the PCI group underwent intravascular ultrasound (IVUS), rotational atherectomy (RA), or both during PCI, according to the physician's experience. All lesions were treated with drug-eluting stents including Firebird II (Microport Co. Shanghai, CN), Xience v (Abbott Co. Santa Clara, USA) and Endeavor Resolve (Medtronic Inc. Minneapolis, USA). Fractional flow reserve (FFR)-guided PCI was used for non-occlusive lesions. If FFR >0.80, it indicates that all lesions do not require intervention and can be treated with medicine. If FFR ≤0.75, then the relationship between each lesion and myocardial ischemia was assessed using the continuous pressure retreat technique. On a continuous pressure curve, a sharp increase in pressure across lesions exceeding 10–15 mmHg indicates that the lesion severely restricts blood flow and requires PCI treatment. If the FFR was between 0.75 and 0.80, a decision to undergo interventional treatment was based on the patient's clinical symptoms [6–8]. The patients in the PCI group were also classified into the complete revascularization (CR) subgroup and partial revascularization (PR) subgroup depending on whether all of the target stenosis was successfully treated and achieved a value of FFR >0.90. After stent implantation, FFR was again assessed. An FFR value over 0.9 was considered to be a successful of stent implantation [7,8]. Rotational atherectomy (RA) and intravascular ultrasound (IVUS) were both used depending on the procedure. If patients who selected coronary intervention did not receive successful PCI, they would be assigned to the OMT group and continue to receive medical treatment. All patients were treated with medication according to coronary heart disease, heart failure and other related guidelines. The patients in the PCI group were further classified into the CR subgroup and PR subgroup depending on whether all of the target stenoses of the coronary artery were treated and reached an FFR >0.9 during the PCI. Stents were also implanted after successfully opening chronic total occlusion (CTO) lesions. If the CTO lesions were not opened and the stents not implanted successfully, then they would be placed in the PR subgroup. The detailed steps are shown in Fig. 1.

All patients were followed up for at least 12 months after discharge. Telephone follow-up was carried out every month by an experienced cardiologist. Follow-up covered symptoms and changes in overall health. All patients were required to attend the outpatient follow-up clinic in the 6th month and 12th month. During outpatient follow-up electrocardiography, biochemistry, and echocardiography studies were obtained.

Observation Content

Complications

Complications included main branch occlusion (vessel diameter ≥2.0 mm), severe dissection, in-stent thrombosis, malignant arrhythmia, and severe vascular access complications (severe bleeding, pseudoaneurysm). Stent thrombosis was defined according to guidelines issued by the American Academic Research Association (ARC) [9, 10].

Secondary Endpoint Events

Angina pectoris and cardiac function were evaluated according to the grading criteria of Canadian Cardiovascular Society (CCS) angina pectoris and New York Heart Association (NYHA) systolic heart failure [11,12].

Primary Endpoint Events

The primary endpoint events included MACCEs: total death (periprocedural death, death in follow-up period), revascularization, stroke, and nonfatal myocardial infarction (MI).

Statistical Analysis

All data were analyzed using SPSS 18.0 software (IBM Corp., Armonk, NY, USA). Continuous variables are presented as means ± standard deviations (SDs), and categorical variables are presented as frequencies and percentages. The comparison of multiple groups was made with one-way analysis of variance and LSD tests. The number of data were expressed by the number of data, and the χ^2 test was used. A statistically significant difference was considered $p < 0.05$.

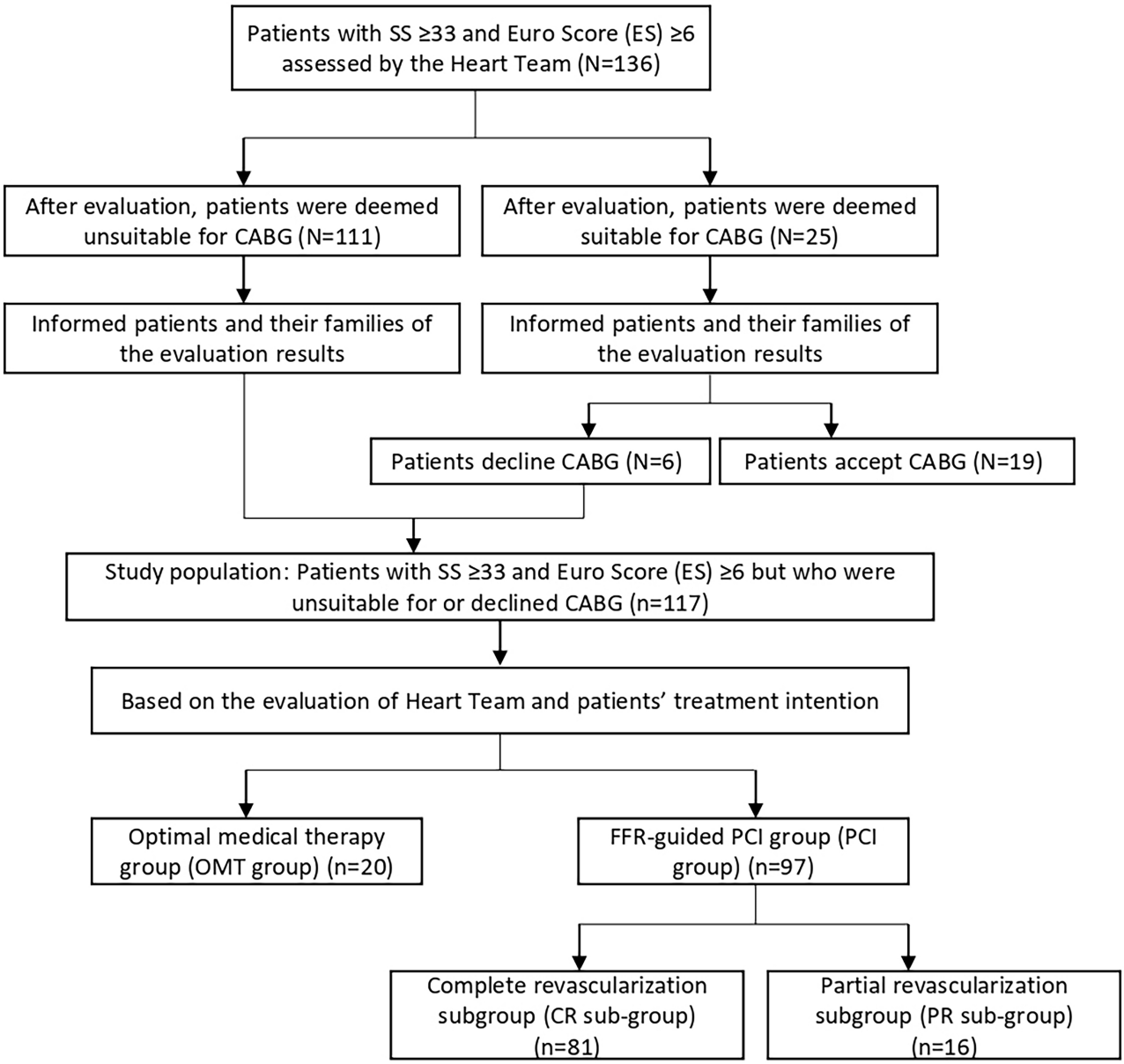

Fig. 1. Flowchart of patient enrollment and grouping. SS, SYNTAX score; ES, Euro Score; CABG, coronary artery bypass graft; OMT group, optimal medical therapy group; FFR-guided, fractional flow reserve-guided; PCI, percutaneous coronary intervention; CR, complete revascularization; PR, partial revascularization.

Results

Baseline Characteristics

The baseline clinical and angiographic data are summarized in Table 1. The results show there were no significant differences in sex distribution, age, or pre-procedural data such as left ventricular end-diastolic dimension (LVEDD), left ventricular end systolic diameter (LVESD), brain natriuretic peptide (BNP), or estimated glomerular filtration rate (eGFR) in the PCI group and OMT groups ($p > 0.05$). The PCI group and OMT group showed no statistically significant difference in the rate of three-vessel lesions, lesion distribution characteristics, and left anterior descending stenoses. In some patients with vascular remodeling, chronic occlusive disease accounted for 31.3% (5/16). There was no significant difference in SS and ES between the PCI group and OMT group ($p > 0.05$).

Compared between the PCI group and OMT group, there was no significant difference in sex distribution, age and pre-procedural data such as LVEDD, LVESD, BNP and eGFR ($p > 0.05$). Although the incidence of three-vessel disease and left anterior descending artery disease in the OMT group were slightly higher than those in PCI group, there was no statistical difference in these parame-

Table 1. Clinical data and coronary angiographic characteristics.

Variable	PCI group (n = 97)				OMT group (n = 20)	#p-value
	CR group	PR group	Group total	p-value		
Number (male/female)	81 (65/16)	16 (10/6)	97 (75/22)	0.56	20 (13/7)	0.27
Age (years)	72.3 ± 12.4	72.7 ± 13.9	72.4 ± 12.9	0.23	71.8 ± 11.5	0.15
Main comorbidities (n, %)						
Hypertension	23 (28.4)	7 (43.8)	30 (30.9)	0.31	9 (45.0)	0.11
Pulmonary disease	12 (14.8)	3 (25.0)	15 (15.5)	0.19	4 (30.9)	0.07
Diabetes	6 (7.4)	3 (1.9)	9 (9.3)	0.15	3 (20.0)	0.09
Renal insufficiency	5 (6.2)	3 (1.9)	8 (8.2)	0.16	2 (20.0)	0.09
Dyslipidemia	14 (17.3)	5 (31.3)	19 (19.6)	0.21	5 (25.0)	0.13
SBP at admission	154.8 ± 19.4	151.3 ± 17.3	153.2 ± 18.5	0.12	156.2 ± 17.5	0.08
DBP at admission	100.2 ± 14.4	101.2 ± 13.8	100.9 ± 13.1	0.11	100.9 ± 11.8	0.10
BMI	26.5 ± 9.4	25.7 ± 9.9	25.7 ± 9.9	0.22	25.8 ± 9.1	0.07
LVEDD	58.7 ± 9.4	57.2 ± 8.7	58.5 ± 9.2	0.19	58.1 ± 9.8	0.09
LVESD	48.3 ± 7.9	49.1 ± 8.5	48.4 ± 8.0	0.18	48.7 ± 8.1	0.08
LVEF	45.4 ± 6.7	44.9 ± 5.2	45.3 ± 5.9	0.16	45.6 ± 6.1	0.07
BNP	1252.7 ± 237.7	1267.7 ± 245.2	1255.2 ± 240.8	0.32	1312.7 ± 257.1	0.22
eGFR	99.7 ± 27.9	103.5 ± 30.1	100.3 ± 28.1	0.57	93.1 ± 21.1	0.12
Lesions distribution (n, %)						
LMCA	23 (28.4)	8 (50.0)	31 (32.0)	0.11	7 (35.0)	0.11
LAD	53 (65.4)	12 (75.0)	65 (67.0)	0.21	15 (75.0)	0.34
LCX	29 (35.8)	10 (62.5) *	39 (40.2)	0.03*	11 (55.0)	0.29
RCA	37 (45.7)	13 (81.3) *	50 (51.5)	0.02*	14 (70.0)	0.06
Bridge vessels	2 (2.5)	1 (6.25)	3 (3.1)	0.07	1 (5.0)	0.11
CTO	9 (11.1)	5 (31.3) *	14 (14.3)	0.01*	3 (15.0)	0.16
SYNTAX score	41.2 ± 6.3	49.2 ± 7.3	42.5 ± 6.5	0.16	46.5 ± 5.9	0.23
Euro score	7.2 ± 1.4	7.9 ± 1.8	7.3 ± 1.6	0.06	7.5 ± 1.7	0.10

Note: Compared between the PCI group and OMT group, # $p > 0.05$. but LCX, RCA and CTO in CR sub-group and PR sub-group, *$p < 0.05$. SBP, Systolic blood pressure; DBP, Diastolic blood pressure; BMI, body mass index; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end systolic diameter; LVEF, left ventricular injection fraction; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; LMCA, left main coronary artery; CTO, chronic total occlusion; LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex coronary artery.

ters. Compared within the PCI group, there was no significant difference in sex distribution, age and pre-procedural data such as LVEDD, LVESD, BNP, eGFR, SS and ES between CR group and PR group (*$p > 0.05$); but there was a significant difference in the distribution of lesions and the incidence of CTO (*$p < 0.05$).

Complications in the PCI Group

In terms of vascular access complications, 10 cases (10/97) had various degrees of hematoma and pressure blister at the puncture sites, which recovered within one week after treatments. No acute or sub-acute thrombosis events or serious malignant arrhythmia events occurred during periprocedural coronary stenting, and no important side branches were occluded during the procedures. Coronary artery perforation and subsequent cardiac tamponade were observed in 1 case, due to rotational atherectomy for a severely calcified lesion, and the perforated coronary artery became occluded spontaneously after balloon occlusion and pericardiocentesis.

There was no significant difference in red blood cell count, platelet count, myocardial enzyme levels, or renal function before or after the procedure in the PCI group ($p > 0.05$, Table 2).

Follow Up after Discharge

Primary Endpoint Events

A total of 18 cases of MACCEs were observed in the PCI group and the incidence was 18.6% (18/97), of which 2 cases died, accounting for 2.1% (1 case in CR subgroup, 1 case in PR subgroup, and the cause of death was possible stent thrombosis), and 9 cases required revascularization. A total of 12 cases of MACCEs occurred in the OMT group and the incidence was 60% (12/20), of which 3 cases died and accounted for 15% (2 cases were acute myocardial infarction and 1 case was malignant arrhythmia). Except for revascularization, there were statistical differences in other aspects such as all-cause mortality, and nonfatal myocardial infarction between PCI group and OMT group ($p < 0.05$, Table 3).

Table 2. Comparison of red blood cell count, platelet count, myocardial enzyme levels, or renal function before and after procedure in PCI group.

TIME	RBC ($\times 10^9$/L)	PLT ($\times 10^9$/L)	CK (IU/L)	CK-MB (IU/L)	eGFR (mL/min)
Pre-PCI	$3.89 \pm 0.98^*$	$178.7 \pm 35.8^{\&}$	$271.7 \pm 51.6^{\#}$	$30.4 \pm 5.3^{\blacksquare}$	$100.3 \pm 28.7^{\blacktriangle}$
Post-PCI 24 h	$3.51 \pm 0.58^*$	$151.2 \pm 29.7^{\&}$	$268.7 \pm 45.1^{\#}$	$31.9 \pm 4.8^{\blacksquare}$	$96.5 \pm 24.2^{\blacktriangle}$
Post-PCI 72 h	$3.77 \pm 0.61^*$	$168.7 \pm 35.2^{\&}$	$224.1 \pm 31.6^{\#}$	$27.6 \pm 5.2^{\blacksquare}$	$101.8 \pm 25.1^{\blacktriangle}$
Post-PCI 7 days	$3.79 \pm 0.71^*$	$171.7 \pm 30.6^{\&}$	$278.7 \pm 35.8^{\#}$	$26.9 \pm 5.5^{\blacksquare}$	$105.1 \pm 29.6^{\blacktriangle}$

Note: $^{\blacksquare}p > 0.05$, $^{\blacktriangle}p > 0.05$, $^{\#}p > 0.05$, $^*p > 0.05$, $^{\&}p > 0.05$, There was no significant difference in red blood cell count, platelet count, myocardial enzyme spectrum, or renal function before or 24 h, 72 h, and 7 days after the procedure in the PCI group. PCI, percutaneous coronary intervention; RBC, red blood cell; CK, Creatine Kinase.

Table 3. Comparison of MACCEs between PCI group and OMT group.

Variable	PCI group (n = 97)			*p* value	OMT group (n = 20)	*p* value
	CR sub-group (n = 81)	PR sub-group (n = 16)	Group total			
MACCEs	10 (10.3)	8 (50.0)	18 (18.6)	0.000^*	12 (60)	$0.000^{\#}$
All-cause mortality	1 (1.0)	1 (6.3)	2 (2.1)	0.750	3 (15)	$0.009^{\#}$
Nonfatal MI	2 (2.5)	1 (6.3)	3 (3.1)	0.559	3 (15)	$0.036^{\#}$
Revascularization	5 (6.2)	4 (25.0)	9 (9.3)	0.068	2 (10)	0.985
Stroke	2 (2.5)	2 (12.5)	4 (4.1)	0.282	4 (20)	$0.009^{\#}$

Note: $^{\#}p < 0.01$, There was a significant difference in MACCEs between PCI group and OMT group; $^*p < 0.01$, There was a significant difference in MACCEs between CR sub- group and PR sub- group. MACCEs, major adverse cardiac and cerebrovascular events; MI, myocardial infarction.

Complications in the terms of vessel such as bleeding at the puncture site have achieved good healing. During the follow-up period, stent restenosis in the PCI group was treated with drug-coated balloons and identified as a MACCE. All stroke events in PCI group and OMT groups did not have a significant impact on the patient's nervous system and quality of life.

Secondary Endpoint Events

The symptoms of angina and heart function in the PCI group were significantly improved and the exercise tolerance was enhanced ($p < 0.05$). In terms of cardiac remodeling, LVEDD, LVESD, LVEF, and cardiac output (CO) in the PCI group were significantly better than in the OMT group ($p < 0.05$), and the degree of improvement in the CR subgroup was greater than in the PR subgroup ($p < 0.05$). The changes in angina, heart function, and cardiac remodeling are shown in Table 4.

Discussion

Patients with atherosclerotic diseases often simultaneously suffer from cardiovascular and cerebrovascular disease, diabetes mellitus, chronic kidney disease, or pulmonary disease. It is generally believed that the main factors affecting the outcome of PCI are the anatomic complexity of coronary lesions, the left ventricular ejection fraction, and the renal function. However, the outcome of CABG is highly susceptible to patients' overall status including age, clinical complications, and similar factors. Various evaluation methods such as SS and ES play an important role in guiding the treatment strategy of CHD. SS can predict the incidence of MACCE after PCI [12] and ES can predict the short- and long-term mortality and other postoperative adverse events after CABG [13]. Generally speaking, if SS is more than 33 and ES can be classified as low risk, CABG should be chosen [14,15]. But if ES $\geq$6 and the predicted mortality rate is more than 10%, CABG mortality is also higher [16,17]. Thus, there is no evidence-based medical recommendation for determining the optimal treatment strategy for the patients with SS $\geq$33 and ES $\geq$6.

In the FAME study, FFR was used to evaluate the physiological function of the lesion and determine the hemodynamic relevance of coronary artery stenosis [18, 19]. It was demonstrated that 2/3 of coronary artery stenoses in which the degree of stenosis exceeded 50% did not cause myocardial ischemia. For left main coronary artery disease, approximately 1/5 of stenoses with a diameter of less than 50% will cause myocardial ischemia [20–22]. This phenomenon is called "image mismatch function" [23]. Because of this phenomenon, it is difficult to determine whether patients with a degree of stenosis of 50–90% should undergo PCI by relying on the results of coronary angiography alone. Therefore, physiological functional evaluation and intravascular imaging techniques can help physicians choose and optimize intervention strategies, thus reducing intraprocedural complications and major adverse cardiovascular events and improving the short- and long-

Table 4. Changes in angina pectoris, heart function and cardiac remodeling.

Variable	PCI group (n = 85[#])						OMT Group (n = 17[#])		
	CR sub-group (n = 80[#])			PR sub-group (n = 15)					
	Pre-PCI	Post-PCI 6 months	Post-PCI 12 months	Pre-PCI	Post-PCI 6 months	Post-PCI 12months	Pre-OMT	Post-OMT 6 months	Post-OMT 12months
CCS (n, %)									
1 grade	13 (16.3)	16 (20)	30 (37.5) *	6 (40)	8 (53.3)	7 (46.7)	1 (5.9)	1 (5.9)	1 (5.9)
2 grade	21 (26.3)	27 (33.8) *	18 (22.5)	4 (26.7)	6 (40) *	7 (46.7) *	3 (17.6)	1 (5.9)	0 (0)
3 grade	28 (35.0)	25 (31.3)	12 (15.0) *	5 (33.3)	1 (6.6) *	1 (6.6)	7 (41.2)	8 (47.1)	9 (52.9)
4 grade	18 (22.5)	12 (15.0) *	10 (12.5) *	1 (6.6)	1 (6.6)	1 (6.6)	9 (52.9)	10 (58.8)	10 (58.8)
NYHA (n, %)									
I grade	9 (11.3)	17 (21.3) *	27 (33.8) *	1 (6.7)	3 (20.0) *	4 (26.7) *	5 (29.4)	3 (17.6)	3 (17.6)
II grade	31 (38.8)	44 (55.0) *	44 (55.0) *	4 (26.7)	7 (46.7)	8 (53.3)	3 (17.6)	4 (23.5)	4 (23.5)
III grade	30 (37.5)	11 (13.8) *	6 (7.5) *	6 (40.0)	3 (20.0) *	3 (20.0) *	6 (35.3)	7 (41.2)	5 (29.4)
IV grade	10 (12.5)	8 (10.0)	3 (3.8) *	5 (33.3)	3 (20.0)	3 (20.0)	3 (17.6)	3 (17.6)	5 (29.4)
LVEDD (mm)	55.7 ± 10.2	48.6 ± 9.1*▲	46.7 ± 9.3*△▲	55.8 ± 10.4	52.7 ± 10.5*▲	50.7 ± 9.8*▲	55.3 ± 11.3	52.3 ± 10.2	52.7 ± 11.7
LVESD (mm)	47.6 ± 9.5	38.1 ± 4.5*▲	36.6 ± 7.5*△▲	48.8 ± 9.7	42.6 ± 8.5*▲	40.6 ± 7.5*▲	42.6 ± 9.5	42.3 ± 9.1	43.1 ± 8.6
LVEF (%)	48.7 ± 9.2	50.1 ± 9.6*▲	51.1 ± 9.7*△▲	47.7 ± 8.6	48.7 ± 4.2*▲	46.7 ± 6.8*▲	47.7 ± 9.2	48.1 ± 8.7	46.1 ± 6.5
CO (mL)	7.6 ± 2.5	8.9 ± 3.7*▲	9.1 ± 3.5*△▲	7.2 ± 2.1	7.6 ± 2.5*▲	7.4 ± 2.7*▲	7.6 ± 2.5	7.4 ± 2.3	7.1 ± 2.5
SV (mL)	57.6 ± 13.1	67.6 ± 16.1*▲	70.2 ± 15.4*△▲	55.6 ± 11.1	61.6 ± 13.5*▲	62.5 ± 12.7*▲	57.3 ± 11.7	56.7 ± 12.6	57.3 ± 13.1
BNP	1246.8 ± 213.1	1036.5 ± 244.1*▲	966.8 ± 211.4*△▲	1316.8 ± 233.3	1126.8 ± 213.4*▲	1046.8 ± 213.1*▲	1306.8 ± 253.1	1416.8 ± 243.1	1536.2 ± 313.1

Note: Comparison with this group before procedure, *$p < 0.05$; Comparison with the same PR group at the same time point, $^{\triangle}p < 0.05$; Comparison with the OMT group at the same time point, $^{\blacktriangle}p < 0.05$; [#]because the patient died during the follow-up, the related parameters could not be collected. BNP, brain natriuretic peptide; NYHA, New York Heart Association; CO, cardiac output; SV, stroke volume; CCS, Canadian Cardiovascular Society.

term efficacy [24–26]. At the same time, the immediate endpoint and forward prognosis of PCI can be optimized by IVUS, FFR, or both. The results of the ILUMIEN III study suggest that intravascular imaging can be used to more accurately select the size of the stent and prevent stent malapposition, and coronary dissection, which can also help in the selection of antithrombotic therapy for some patients, especially those with higher thrombotic or bleeding risk or a need to undergo surgery [27].

This retrospective study also showed that frequency and duration of angina, heart function, activity tolerance, and the total mortality rate, revascularization, stroke, and nonfatal myocardial infarction such as MACCEs in patients with SS $\geq$33 but unsuitable for CABG, which was performed with PCI under the guidance of FFR, had results that were significantly better than those in the OMT group. The benefit was not only reflected in the CR subgroup but also in the PR subgroup. The results of this clinical retrospective analysis suggest that although there may be a certain degree of ischemic clinical symptoms for some patients with revascularization, the risk of major cardiac events, will be greatly reduced. Furthermore, the results showed that LVEDD, LVESD, LVEF, and CO in the PCI treatment group were significantly better than those in the OMT group, which was consistent with other studies [28–31].

There are indeed many interrelated clinical factors that influence each other and result in different outcomes. However, the main purpose of this retrospective study provide assistance in treatment strategies. In clinical practice, the selection of treatment strategies is mainly based on these two scores—SYNTAX score and Euro Score rather than a single influencing factor now. This opinion was also recommended in the now guidelines. That is to say, decisions of treatment strategies are not based on a single clinical factor but comprehensive factors. The main purpose of this study is to provide assistance for the treatment decision-making of coronary heart disease patients rather than study whether these influencing factors have an impact on coronary heart disease. Moreover, these scoring methods have covered multiple clinical factors. Intervention or surgical methods are not decided by a single factor but a comprehensive scoring result. Furthermore, there was no significant difference in single clinical factors between different groups of patients in this study. So, it has little impact on the research conclusions.

These types of patients inevitably would be encountered in clinical practice, and the specific treatment guidelines for these patients do not provide clear recommendations. Future research will compare the clinical benefits of these three treatment methods, drug optimization therapy recommended by the guidelines, PCI optimization therapy and CABG. It will be necessary to design a multicenter, randomized double-blind controlled study protocol to further determine the clinical significance of the finding of our study.

Study Limitations

Because this is a single-center retrospective analysis, the sample size was small which impacts the results of the study. Therefore, these findings need to be verified by multicenter prospective studies. In addition, the factors that affect the treatment effectiveness of patients in clinical practice are complex. In this study, selecting only the currently recognized relevant factors for analysis and comparison may result in an incomplete analysis. However, scoring tools such as the SYNTAX score and the Euro Score, take into account many clinical factors, which can improve the accuracy of our conclusions.

Conclusions

Based on optimal medical therapy, FFR-guided PCI can confer some clinical benefit to coronary artery disease patients with SS $\geq$33 and ES $\geq$6 who were unsuitable for or declined CABG. Even in the PR group, FFR-guided PCI can alleviate the clinical symptoms of angina pectoris, which is helpful for improving their quality of life.

Availability of Data and Materials

The data that support the findings of this study are available on request from the corresponding author upon reasonable request.

Author Contributions

ZW conceptualized the study and responsible for interpretation of the study. XC, YZ, NG, ZC acquired the data and responsible for data analysis. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki, and this protocol was approved the ethics committee of Jiangxi Provincial People's Hospital (approval number: KT003). All subjects gave their informed consent for inclusion before they participated in the study.

Acknowledgment

Professor Lang Hong provides technical assistance in PCI.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, *et al*. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2005; 1: 219–227.

[2] Haberal I, Balli M, Tekin EE, Uysal A, Ozsoy SD, Yesiltas MA, *et al*. SYNTAX and Coronary Artery Calcium Score Predict Atherosclerotic Plaque Formation in the Ascending Aorta. The Heart Surgery Forum. 2021; 2021: E996–E1004.

[3] Peng C, Wu H, Kim S, Dai X, Jiang X. Recent Advances in Transducers for Intravascular Ultrasound (IVUS) Imaging. Sensors (Basel, Switzerland). 2021; 21: 3540.

[4] Reiber JH, Tu S, Tuinenburg JC, Koning G, Janssen JP, Dijkstra J. QCA, IVUS and OCT in interventional cardiology in 2011. Cardiovascular diagnosis and therapy. 2011; 1: 57–70.

[5] Dykun I, Babinets O, Hendricks S, Balcer B, Puri R, Al-Rashid F, *et al*. Utilization of IVUS improves all-cause mortality in patients undergoing invasive coronary angiography. Atherosclerosis Plus. 2021; 43: 10–17.

[6] Lee JM, Shin E, Nam C, Doh J, Hwang D, Park J, *et al*. Clinical Outcomes According to Fractional Flow Reserve or Instantaneous Wave-Free Ratio in Deferred Lesions. JACC: Cardiovascular Interventions. 2017; 10: 2502–2510.

[7] Reuter H, Baldus S. FFR-gesteuerte Revaskularisation – wann indiziert, wann überflüssig? DMW - Deutsche Medizinische Wochenschrift. 2017; 142: 1595–1603.

[8] van Nunen LX, Zimmermann FM, Tonino PAL, Barbato E, Baumbach A, Engstrøm T, *et al*. Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. Lancet. 2015; 386: 1853–1860.

[9] Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es G, *et al*. Clinical End Points in Coronary Stent Trials. Circulation. 2007; 115: 2344–2351.

[10] Lemesle G, Delhaye C, Bonello L, de Labriolle A, Waksman R, Pichard A. Stent thrombosis in 2008: Definition, predictors, prognosis and treatment. Archives of Cardiovascular Diseases. 2008; 101: 769–777.

[11] McGillion M, Arthur HM, Cook A, Carroll SL, Victor JC, L'Allier PL, *et al*. Management of Patients with Refractory Angina: Canadian Cardiovascular Society/Canadian Pain Society Joint Guidelines. Canadian Journal of Cardiology. 2012; 28: S20–S41.

[12] Serruys PW, Morice M, Kappetein AP, Colombo A, Holmes DR, Mack MJ, *et al*. Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease. New England Journal of Medicine. 2009; 360: 961–972.

[13] Toumpoulis IK, Anagnostopoulos CE, DeRose JJ, Swistel DG. European system for cardiac operative risk evaluation predicts long-term survival in patients with coronary artery bypass grafting. European Journal of Cardio-Thoracic Surgery. 2004; 25: 51–58.

[14] Head SJ, Davierwala PM, Serruys PW, Redwood SR, Colombo A, Mack MJ, *et al*. Coronary artery bypass grafting vs. percutaneous coronary intervention for patients with three-vessel disease: final five-year follow-up of the SYNTAX trial. European Heart Journal. 2014; 35: 2821–2830.

[15] Takahashi K, Serruys PW, Gao C, Ono M, Wang R, Thuijs DJFM, *et al*. Ten-Year all-Cause Death According to Completeness of Revascularization in Patients with Three-Vessel Disease or Left Main Coronary Artery Disease: Insights from the SYNTAX Extended Survival Study. Circulation. 2021; 144: 96–109.

[16] Alam M, Huang HD, Shahzad SA, Kar B, Virani SS, Rogers PA, *et al*. Percutaneous Coronary Intervention vs. Coronary Artery Bypass Graft Surgery for Unprotected Left Main Coronary Artery Disease in the Drug-Eluting Stents Era. Circulation Journal. 2013; 77: 372–382.

[17] Mohr FW, Morice M, Kappetein AP, Feldman TE, Ståhle E, Colombo A, *et al*. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet. 2013; 381: 629–638.

[18] Pijls NH, Fearon WF, Tonino PA, Siebert U, Ikeno F, Bornschein B, *et al*. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease: 2-year follow-up of the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study. Journal of the American College of Cardiology. 2010; 56: 177–184.

[19] Tonino PA, Fearon WF, De Bruyne B, Oldroyd KG, Leesar MA, Ver Lee PN, *et al*. Angiographic versus functional severity of coronary artery stenoses in the FAME study fractional flow reserve versus angiography in multivessel evaluation. Journal of the American College of Cardiology. 2010; 55: 2816–2821.

[20] Patel MR, Calhoon JH, Dehmer GJ, Grantham JA, Maddox TM, Maron DJ, *et al*. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 Appropriate Use Criteria for Coronary Revascularization in Patients With Stable Ischemic Heart Disease: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. Journal of the American College of Cardiology. 2017; 69: 2212–2241.

[21] White CW, Wright CB, Doty DB, Hiratza LF, Eastham CL, Harrison DG, *et al*. Does Visual Interpretation of the Coronary Arteriogram Predict the Physiologic Importance of a Coronary Stenosis? New England Journal of Medicine. 1984; 310: 819–824.

[22] Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, *et al*. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percu-

taneous Cardiovascular Interventions (EAPCI). European heart journal. 2014 ;35: 2541–2619.

[23] Adjedj J, Stoyanov N, Muller O. Comparison of coronary angiography and intracoronary imaging with fractional flow reserve for coronary artery disease evaluation: An anatomical-functional mismatch. Anatolian journal of cardiology. 2018; 20: 182–189.

[24] Zhang J, Gao X, Kan J, Ge Z, Han L, Lu S, *et al*. Intravascular Ultrasound Versus Angiography-Guided Drug-Eluting Stent Implantation. Journal of the American College of Cardiology. 2018; 72: 3126–3137.

[25] Budrys P, Peace A, Baranauskas A, Davidavicius G. Intravascular Ultrasound *vs*. Fractional Flow Reserve for Percutaneous Coronary Intervention Optimization in Long Coronary Artery Lesions. Diagnostics (Basel, Switzerland). 2023; 13: 2921.

[26] Kong MG, Han J, Kang J, Zheng C, Yang H, Park KW, *et al*. Clinical outcomes of long stenting in the drug-eluting stent era: patient-level pooled analysis from the GRAND-DES registry. EuroIntervention. 2021; 16: 1318–1325.

[27] Konstantinidis NV, Werner GS, Deftereos S, Di Mario C, Galassi AR, Buettner JH, *et al*. Temporal Trends in Chronic Total Occlusion Interventions in Europe. Circulation: Cardiovascular Interventions. 2018; 11: e006229.

[28] Xenogiannis I, Choi JW, Alaswad K, Khatri JJ, Doing AH, Dattilo P, *et al*. Outcomes of subintimal plaque modification in chronic total occlusion percutaneous coronary intervention. Catheterization and Cardiovascular Interventions. 2020; 96: 1029–1035.

[29] Tanaka H, Tsuchikane E, Muramatsu T, Kishi K, Muto M, Oikawa Y, *et al*. A Novel Algorithm for Treating Chronic Total Coronary Artery Occlusion. Journal of the American College of Cardiology. 2019; 74: 2392–2404.

[30] Katoh H, Yamane M, Muramatsu T, Okamura A, Kashima Y, Matsuno S, *et al*. Safety of Percutaneous Coronary Intervention for Chronic Total Occlusion in Patients with Multi-Vessel Disease: Sub-Analysis of the Japanese Retrograde Summit Registry. Cardiovascular Revascularization Medicine. 2021; 25: 36–42.

[31] Maeremans J, Walsh S, Knaapen P, Spratt JC, Avran A, Hanratty CG, *et al*. The Hybrid Algorithm for Treating Chronic Total Occlusions in Europe: The RECHARGE Registry. Journal of the American College of Cardiology. 2016; 68: 1958–1970.